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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/815,388 | 03/31/2004 | Pablo Caviedes | USF-167XC1 | 7583 |

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| EXAMINER | |
|---|---|
| FORD, ALLISON M | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1651 | |

DATE MAILED: 04/05/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/815,388 | CAVIEDES ET AL. | |
| | Examiner | Art Unit | |
| | Allison M. Ford | 1651 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☐ Responsive to communication(s) filed on *2/2/06*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *18,19,21-26,30,31 and 33-43* is/are pending in the application.

4a) Of the above claim(s) *40-43* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *18,19,21-26,30,31 and 33-39* is/are rejected.

7)☒ Claim(s) *19,23 and 33* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *31 March 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

## DETAILED ACTION

### *Response to Amendments*

Applicant's amendments filed 2 February 2006 to claims 18, 19, 21, 25, 26 and 30 have been entered. Claims 1-17, 20, 27-29 and 32 have been cancelled. Claims 33-43 have been added. Claims 18, 19, 21-26, 30, 31 and 33-43 remain pending in the current application, with claims 40-43 being withdrawn from consideration as being directed to a non-elected invention. Claims 18, 19, 21-26 and 30-39 have been considered on the merits.

### *Claim Objections*

Claim 23 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. In the instant case, claim 23 is dependent on parent claim 21, which requires the solid substrate to comprise polystyrene and have an untreated surface for supporting said culture medium; claim 23 fails to limit parent claim 21 because it requires the solid substrate to comprise untreated plastic. Polystyrene is a type of plastic, since the parent claim 21 requires polystyrene with at least one untreated surface, it effectively *is* untreated plastic, and thus claim 23 fails to add anything to the claim.

Furthermore, regarding claims 19 and 33, applicant is advised that should either of claims 19 or 33 be found allowable, the other will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k). In the instant case both claims 19 and 33 are directly dependent on claim 18, and both require the cell culture to be free of calcium; though claim 33 says "lacks calcium ion as a formulated component" as opposed to claim 19

which does not specify calcium ions, one of ordinary skill recognizes that calcium, if provided in any salt form will disassociate to calcium ions, thus both claims are effectively prohibiting calcium ions.

### *Claim Rejections - 35 USC § 112*

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 35 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Applicants' claim 35 is directed to the cell culture of claim 18, wherein all of said neuronal cells within each of said one or more aggregates are living, having not begun to degenerate.

Applicants' claim prohibits any cell, in any of the aggregates, from be dead, dying, or in any way degenerating. One of ordinary skill in the art will recognize that in any cell culture maintained for any substantial length of time, there are constantly cells at all stages of the cell life cycle, including death. It would be infeasible for one to claim a cell culture that contains *zero* dead or dying cells, as death is a natural and necessary part of the cell culture life cycle, absent some substantial step or measure which must be taken to immediately separate and remove all degenerating, dying and dead cells from the culture.

While applicants' claim currently does require complete viability of all cells in the culture, it appears applicants may have intended for the limitation to merely require the aggregates to comprise living neuronal cells, so as to differentiate from cell cultures comprising a monolayer process-forming, neuronal cells where dead cells would disassociate from the substrate and float in the media forming

'aggregates.' Therefore, in order to provide compact prosecution, for purposes of applying prior art, claim 35 will be interpreted as requiring the aggregates to comprise mainly living cells, that remain viable in suspension.

### *Claim Rejections - 35 USC § 112*

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 39 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Applicants' claim 39 is directed to a cell culture comprising process-forming neuronal cells of the central nervous system; and an untreated, polystyrene microbiological plate, wherein said neuronal cells lack processes, are seeded on said plate, and are clustered into one or more aggregates, wherein there is no attachment of said neuronal cells to said plate, and wherein said culture has a calcium concentration of 10uM or less.

It is unclear how the neuronal cells are seeded on the microbiological plate, yet there is no attachment of the neuronal cells to the plate. "Seeding cells *on* a plate" implies attachment, or at the very least, contact between the cells and plate, which the claim prohibits. For purposes of examination that particular limitation ("neuronal cells.. are seeded on said plate") will be ignored, rather it will be assumed the neuronal cells are merely present in the culture.

### *Claim Rejections - 35 USC § 102*

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –

> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 18, 19, 22-26 and 33 are rejected under 35 U.S.C. 102(a) as being anticipated by Andrews et al (Poster presentation from Cell Culture and Engineering Conference in Snowmass, CO; 2002).

Andrews et al teach culturing RCSN-3 cells (rat neurons from the central nervous system) in microbiological plates (which applicant calls a solid substrate which support the culture medium) to produce a mass suspension culture wherein the cells do not adhere to the substrate, but form three-dimensional aggregates. The microbiological plates were plastic, and were untreated by any cell attachment treatments or cell attachment factors (as evidenced by their comparison to 'standard conditions' comprising glass or plastic treated plates). Andrews et al teach the neuronal cells were maintained in an optimized media comprising low serum (2%) supplemented with hormones (insulin, progesterone), proteins (transferrin), and trace elements (Sodium selenite, putrescine). Andrews et al do not teach calcium as a component of the media; therefore, in the absence of any evidence showing calcium was present in the media used by Andrews et al, the media of Andrews et al is considered to be calcium free (Claims 18, 19, 22-26 and 33). Therefore the reference anticipates the claimed subject matter.

### *Claim Rejections - 35 USC § 103*

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 18, 21-26, 30, 31 and 35-39 are rejected under 35 U.S.C. 103(a) as being unpatentable over Takazawa et al (US Patent 5,219,752), in view of Studer et al (WO 00/05343), and further in view of Boss et al (US Patent 5,411,883).

Takazawa et al teach an animal cell culture wherein adherent animal cells are cultured in such conditions so that the cells do not adhere, but remain in suspension as single cells or small cell clumps. Takazawa et al teach the cells remain in suspension as single cells, or in small cell aggregates of 1.1-50 cells on average (which applicant calls not substantially adhering to the substrate) (See Takazawa et al, col. 14, ln 33-43).Takazawa et al teach a wide variety of normally adherent animal cells can be maintained in suspension culture by the means of their invention, the types of cells include several cell types derived from the nervous system, including rat glial cells (a category of neuronal, process-forming cells) (ATCC No. CCL 107) and mouse neuroblastomas (neurons) (ATCC No. CCL 131) (See Takazawa et al, Table spanning col. 5-12).

While Takazawa et al does not specifically process-forming cells of the central nervous system, it would have been obvious to one of ordinary skill in the art at the time the invention was made that the culture method of Takazawa et al was applicable to any normally adherent animal cell cultures, this assertion is based on their extensive, non-limiting list of cell types described as applicable in their claimed methods. It is noted that Takazawa et al does teach process-forming cells from the peripheral nervous system (mouse neuroblastomal cells ATCC No. CCL 131) and other neuronal cells, including cells derived from rat glia (ATCC No. CCL 107); therefore, one of ordinary skill in the art would have expected that neuronal, process-forming cells from the central nervous would also have been within the scope of the invention of Takazawa et al. Methods of culturing process-forming cells from the central nervous system in aggregate cultures were desirable at the time the invention was made, for example, Studer et al teach formation of dopaminergic cells (neuronal process forming cells from the CNS) in aggregate culture is desirable because it allows for recovery of the cultured cells without use of enzymatic

digestion, which may damage the cells (See Studer et al, Pg. 3, ln 16-25). Use of dopaminergic cells in large numbers was desirable for treatment of various diseases and conditions, including Parkinson's, Alzheimer's and Huntington's disease; production of dopaminergic cells in vitro allows for production of a greater number of cells with less ethical concerns (as such cell samples are otherwise obtained from fetuses and 3-5 fetuses are required to accumulate a sufficient number of cells for transplantation) (See Studer et al, Pg. 1, ln 12- Pg 2, ln 11). Alternatively, such process forming neuronal cells from the CNS are also valuable in culture for the proteins and chemical which they secrete. For example, dopaminergic neurons secrete dopamine and tyrosine hydroxylase (See Studer et al, Pg. 8, ln 4-10). Production of such chemicals would be useful for studies on how these drugs affect the body and finding potential therapies for those diseases listed above. Therefore, one of ordinary skill in the art would have been motivated to utilize the suspension culture method of Takazawa et al to produce cultures of dopaminergic cells in suspension culture, thereby creating cell cultures comprising neuronal, process forming cells of the CNS in aggregate form (wherein the cells within the aggregates are living (Claims 35)) which could either be recovered from culture for transplantation in vivo, or maintained in culture for production of drugs and bioactive agents specific to those cells.

The cell culture of Takazawa et al further includes serum-free media with a calcium ion ($Ca^{2+}$) concentration of 0.002 mM to 0.3 mM (2uM to 300uM), preferably 0.02 mM to 0.25mM (20uM to 250uM) (See Takazawa et al col. 13, ln 66-col. 14, ln 17). Though the concentration of calcium ions taught by Takazawa et al has a higher upper limit than that which is currently claimed, at the time of the claimed invention, it would have been well within the purview of one of ordinary skill in the art to optimize the amount calcium ion to be included in the cell culture of Takazawa et al as a matter of routine experimentation (Claims 18, 26, 36-38). Moreover, at the time of the claimed invention, one of ordinary skill in the art would have been motivated by routine practice to optimize the concentration of calcium ions in the cell culture with a reasonable expectation for successfully obtaining a cell culture that can

effectively produce active biological agents secreted from the cultured cells in a higher quantity than possible in adherent cultures within the same culture vessel. Generally, differences in concentration will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical or produces unexpected results. Where the general conditions of a claim are disclosed by the prior art it is not inventive to discover the optimum or workable ranges by routine experimentation, See *In re Aller,* 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955). Specifically note that where the claimed ranges overlap, such as in the instant case, or lie inside ranges disclosed by the prior art a prima facie case of obviousness exists. See *In re Wertheim,* 541 F.2d 257, 191 USPQ 90 (CCPA 1976); *In re Woodruff,* 919 F.2d 1575, 16 USPQ2d 1934 (Fed. Cir. 1990). Therefore, though Takazawa et al claim a calcium ion concentration of 0.002mM to 0.3mM (2uM to 300uM), preferably 0.02mM to 0.25mM (20uM to 250uM) $Ca^{2+}$; it would have been prima facie obvious to optimize this concentration to below 100uM or 50uM.

The cell culture of Takazawa et al further comprised a cell culture vessel (which applicant calls a solid substrate) (See Fig. 1). No cell attachment treatments or cell attachment factors are included; thus the cell culture vessel (solid substrate did not comprise any charged molecules or treatment on its surface). Though Takazawa et al disclose a culture vessel (which applicant calls a solid substrate) and provide a drawing of the culture device, they are silent on the exact material of the culture vessel. The culture vessel of Takazawa et al was designed to automatically cycle the culture medium to and from the cell culture; however, it would have been obvious to one of ordinary skill in the art at the time the invention was made to use a standard, microbiological grade culture vessel, such as a Petri dish, flask, bottle, plate, tube, or vial comprised of untreated polystyrene plastic, as polystyrene is particularly useful for resisting adhesion (See Studer et al, Pg. 9, ln 3-17) (Claims 21-25 and 39). One of ordinary skill in the art would have been motivated to use any form of a microbiological grade culture dish because these types of culture vessels are the standard used in cell culture and are available from a variety of laboratory

product retailers. One would further have been motivated to use such basic culture vessels instead of the automated device of Takazawa et al in order to save money, as an automated machine would be more expensive, and in order to be able to change the culture medium according to the growth rate of the cells, as opposed to a scheduled media change as is done by automated systems. One of ordinary skill in the art would have been motivated to use untreated microbiological grade (as opposed to tissue culture grade) culture vessels so as to prevent/reduce cell adhesion to the solid substrates; as Takazawa et al desire for the cells to not adhere in a monolayer, but stay in a mass suspension (See Takazawa et al col. 1, ln 55-col. 2, ln 16). One would expect success using any suitable, untreated, microbiological grade untreated polystyrene culture dish to create the cell culture of Takazawa et al because the cells of Takazawa et al are not intended to adhere to the substrate, but rather to be prevented from adhering based on the low concentration of calcium. Additionally, because adhesion is not desired, one would expect successfully decreasing adhesion by using culture dishes not treated to promote adhesion.

Regarding the size of the cells aggregates which are formed by the method of Takazawa et al, which can be performed using human dopaminergic cells, such as suggested by Studer et al, Takazawa et al is silent on the size of the aggregates in the suspension. However, at the time the invention was made it would have been well within the purview of one of ordinary to manipulate the size of the cell aggregates. In support, Boss et al teach a similar method of producing aggregates of dopaminergic neuronal cells in suspension culture; Boss et al further teach the size of the aggregates can be adjusted by manipulating the number of cells per culture (by controlling both the number of cells initially seeded and the initial volume of culture medium) (See Boss et al, col. 7, ln 40-54). Boss et al also teach that minimizing the number of necrotic cells in the center of the aggregates helps to ensure lower initial plating densities and maintaining smaller aggregate size. Boss et al teach a slightly lower aggregate size range than Studer et al, of 100um-1000um, as opposed to 0.6-1.2mm (600-1200um) (See Boss et al, col. 5, ln 49-51). The size range of Boss et al encompasses the claimed size range of 150um-200um; please note that cases where the claimed

ranges "overlap or lie inside ranges disclosed by the prior art" a prima facie case of obviousness exists (Claim 34). *In re Wertheim, 541 F.2d 257, 191 USPQ 90 (CCPA 1976); In re Woodruff, 919 F.2d 1575, 16 USPQ2d 1934 (Fed.Cir. 1990).* Therefore, based on the teachings of Boss et al regarding optimization of the size of the aggregates in suspension culture, one of ordinary skill in the art would expect to be able to successfully manipulate the size of neuronal cell aggregates produced by the method of Takazawa et al/Studer et al as desired. One would be motivated to optimize the size of the cell aggregates to a size range appropriate for the intended use. For example, in cases where the neuronal cell aggregates are to be recovered from culture and used in therapeutic treatments involving injection of the dopaminergic cell-containing aggregates directly into the brain of a patient in need thereof, as taught by Studer et al (See Studer et al, Pg 4, ln 32-Pg. 5, ln 3 & Pg. 13, ln 1-Pg. 14, ln 10), Boss et al teach that manipulation of the size of aggregates allows one to formulate the aggregates so that they can pass unobstructed through a needle or catheter (See Boss et al, col. 5, ln 40-51). Therefore, for the therapeutic treatments suggested by Studer et al one would be motivated to manipulate the size of the aggregates formed in the cultures of Takazawa et al, and one would have expected success in doing such optimization, based on the teachings of Boss et al (Claim 34).

Finally, though Takazawa et al do not teach co-culturing dopaminergic cells with a second cell type, wherein the second cell type is either another process-forming cell, such as other neuronal cells, or are non-process-forming cells, it would have been obvious to one skilled in the art at the time the invention was made to include multiple cell types that are capable of growing in the same general culture conditions in order to obtain a mixture of bioactive products from two or more cell types (Claims 30 and 31). Takazawa et al create the suspension culture in order to produce biologically active substances, for example dopamine and tyrosine hydroxylase from dopaminergic cells, in higher concentrations than permitted by adherent culture, based on the fact that more cells per volume can be maintained in suspension culture than can be maintained in adherent culture (See Takazawa et al, col. 4, ln 37-60).

Thus by culturing two or more different cell types together, the collected culture medium will comprise a mixture of growth factors and proteins that can subsequently be used for future cell culture. By culturing two or more cell types together one saves the time and energy on culturing two separate cell populations and then combining the biologically active products obtained therefrom. One of ordinary skill in the art would be motivated to use mixtures including two or more types of process-forming cells or one type of process-forming cell and one type of non-process forming cell in order to create different cocktails of growth mixtures and hormones that would be useful for future cell cultures and experimentations. One would expect success because co-culturing cells is well known in the art; one of ordinary skill would be able to select one or more cell types that could successfully be cultured together with the dopaminergic cells described above, and have a reasonable expectation of successfully obtaining a biologically active substance containing a combination of growth factors and other secreted proteins and hormones from each cell type (for example, dopamine and tyrozine hydroxylase, which are secreted from dopaminergic neurons (See Studer et al, Pg. 8, ln 4-10)). Therefore the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

### *Response to Arguments*

Applicant's arguments filed 2 February 2006 have been fully considered. Only the arguments pertaining to rejections still standing in the case will be addressed.

Regarding the rejection over Andrews et al under 35 USC 102(a) applicants argue that Andrews et al does not teach the claimed calcium concentration, rather Andrews et al is silent with regards to any calcium concentration in the media used, and thus the examiner cannot assume that the media used was 'inherently' the same as that used in the current invention with the same calcium concentration. Additionally, applicants argue that the Andrews et al poster is not applicable as prior art under 102(a), as

current inventors Caviedes, P, Caviedes R, Asenjo, Andrews, and Sepulveda were all authors of the poster.

Regarding the rejection over Takazawa et al under 35 USC 103(a) applicants argue that Takazawa et al does not teach or suggest a cell culture comprising neuronal cells of the CNS, only of the peripheral nervous system. Applicants state Takazawa et al only provide actual evidence of successfully culturing kidney cells, and thus they argue there was no expectation of success for culture of neuronal cells of the CNS in the method of Takazawa et al. Applicants argue that Takazawa et al teach away from the claimed invention, citing Grinstaff et al. Finally applicants argue that their invention has a different motivation not taught or suggested by Takazawa et al.

In response to applicants' argument regarding the calcium concentration of the media in the Andrews et al poster, it is acknowledged that the examiner cannot assume the media described in the poster was one and the same as that used in the present invention, and thus the calcium concentration cannot be assumed to inherently the same. However, it is true that the poster does not teach a calcium concentration, in fact, the poster does not teach the culture medium used in the experiment to comprise calcium at all; therefore, in the absence of any teachings of calcium as a component, it cannot be assumed that calcium was present in the culture medium at al; thus based on the teachings of the poster, the culture medium used was free of calcium. In the absence of any teachings or suggestion that the culture medium described in the poster did, in fact, comprise additional components, including calcium, which are not listed, it cannot be assumed that any components except insulin, progesterone, transferrin, sodium selenite and putrescine were present in the medium.

In response to applicants' argument that the Andrews et al disclosure is not available as prior art under 35 USC 102, as it was not 'by another' based on overlapping authors/inventors, applicant is reminded that "Others" means any combination of authors or inventors different than the inventive entity

> The term "others" in 35 U.S.C. 102(a) refers to any entity which is different from the inventive entity. The entity need only differ by one person to be "by others." This holds true for all types of references eligible as prior art under 35 U.S.C. 102(a) including publications as well as public knowledge and use. Any other interpretation of 35 U.S.C. 102(a) "would negate the one year [grace] period afforded under § 102(b)." In re Katz, 687 F.2d 450, 215 USPQ 14 (CCPA 1982).

Therefore, because T. Freeman, C. Arrigada, and J. Rivera are inventors on the instant application, but are not authors on the Andrews et al work, and because P. Venegas is an author on the Andrews et al work, but is not an inventor on the instant application, the Andrews et al is considered "by another" and is appropriately applied under 102(a). The declaration provided by Dr. Caviedes does not serve as an appropriate declaration or petition to add or remove inventors from the present application, and thus has no effect on changing the status of the Andrews et al work as applicable prior art.

In response to applicants' arguments that Takazawa et al do not teach neuronal cells from the central nervous system, as now recited in claim 18, the rejection has been amended to show that culture of any normally adherent animal cell would have been within the scope of the teachings of Takazawa et al. Furthermore, motivation has been provided, relying on Studer et al, to show that it was desired at the time the invention was made to create suspension cultures of neuronal cells from the CNS, such as dopaminergic cells. Regarding applicants argument that Takazawa et al teaches away from the claimed invention, it is not clear what applicant is relying on as a teaching away. Applicants cite Grinstaff et al, who teaches human fibroblasts and HUVEC do adhere to untreated polystyrene; however, it is noted, first, that the examiner is not arguing human fibroblasts or HUVECs, and second, that Grinstaff et al is not comparable to Takazawa et al because Takazawa et al rely on adjustment of calcium concentration to prevent adherence, whereas Grinstaff et al does not manipulate calcium concentrations, but relies solely on untreated polystyrene. Furthermore, in response to applicants' argument that Takazawa et al is not enabled for all types of adherent animal cells, relying on the fact that Takazawa et al have only showed a single experiment with kidney cells, please note that when considering the factors relating to

determination of non-enablement, if all the other factors point towards enablement, then the absence or low number of working examples will not by itself render the invention non-enabled. To present a valid reason why the teachings of Takazawa et al are not valid for their entire disclosed scope one must evaluate all the facts and evidence and state why one would not expect to be able to extrapolate the one working example across the entire scope of the invention.

Finally, in response to applicants' argument that Takazawa et al does not teach suspension culture of neuronal process forming cells of the CNS for the arrest of neurite extension to prevent cell death by axotomy (the intention of the present invention), please note the reason or motivation to modify the reference may often suggest what the inventor has done, but for a different purpose or to solve a different problem. It is not necessary that the prior art suggest the modification to achieve the same advantage or result discovered by applicant. *In re Linter*, 458 F.2d 1013, 173 USPQ 560 (CCPA 1972); *In re Dillon*, 919 F.2d 688, 16 USPQ2d 1897 (Fed. Cir. 1990), cert. denied, 500 U.S. 904 (1991). Although Ex parte Levengood, 28 USPQ2d 1300, 1302 (Bd. Pat. App. & Inter. 1993) states that obviousness cannot be established by combining references "without also providing evidence of the motivating force which would impel one skilled in the art to do what the patent applicant has done" (emphasis added), reading the quotation in context it is clear that while there must be motivation to make the claimed invention, there is no requirement that the prior art provide the same reason as the applicant to make the claimed invention; in the instant case, the examiner has provided appropriate motivation and thus the rejection remains proper.

### *Conclusion*

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

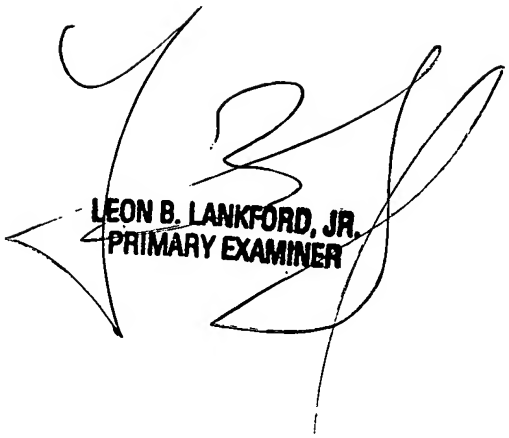
A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Allison M. Ford whose telephone number is 571-272-2936. The examiner can normally be reached on 7:30-5 M-Th, alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Allison M Ford
Examiner
Art Unit 1651


LEON B. LANKFORD, JR.
PRIMARY EXAMINER